## REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 CFR § 1.112, and in light of the remarks which follow are respectfully requested.

By the present amendments, the non-elected claims are cancelled to expedite prosecution. It is anticipated that this amendment and the remarks below shall place the case in condition for allowance.

Claim 97 has been amended to merely recite expression of the recited genes and does not require that the expression thereof inhibit cell differentiation. This amendment does not raise new matter issues as the specification at least provides written description support for transfecting and expressing these genes in CICM cell line.

Turning now to the Office Action, the Examiner is thanked for the withdrawal of most of the prior objections and rejections.

The comments concerning non-elected claims are moot as these claims are cancelled to expedite prosecution.

Similarly, the comments concerning claims 101 and 102 are moot as they are cancelled to expedite prosecution. However, it is respectfully submitted that the claims are not duplications of claim 91.

Claims 91-105 stand rejected under 35 USC § 112 first paragraph, new matter grounds. This rejection is respectfully traversed.

The Examiner, based on the rejection, seems to be of the view that the as-filed specification does not provide written description support for a cell culture comprising genetically identical cells, except for the expression, or absence of expression of a particular transgene. Rather, the Examiner suggests that the disclosure only provides support for "composition of cells which [are] *sic* genetically different which were combined to provide a chimeric composition of cells." This rejection is respectfully traversed.

It is noted at the outset that all the disclosed methods for producing transgenic CICM cell lines start with genetically identical cells (derived from a NT unit), which are then transfected with a transgene that expresses a desired gene.

Therefore, unless transfection and selection is 100%, the method will inevitably give rise to a genetically identical population of cells except for the fact that some will contain and express the transgene and some will not. Additionally, even with respect to those that contain the transgene, while otherwise genetically identical, expression will inevitably vary dependent on where the transgene becomes stably integrated. This is a known consequence, which is in fact associated with producing any transgenic cell line wherein the starting material comprises cells having a particular and shared genotype.

It would appear that the Examiner may have made the rejection based on the fact that the disclosure allegedly does not provide literal support for the claims.

However, this is not the legal standard. All that the law requires is that the specification clearly convey that the inventors were in possession of the invention based on the as-filed application. This legal standard is more than adequately satisfied based on the as-filed disclosure, the examples.

Note, e.g., the table at page 41 which quantifies the percent efficiency of the formation of transgenic cell colonies and the text of the example which acknowledges that a selection procedure [for transgenic cells] was required [G418 selection] and was not entirely [100%] selective under specific G418 concentrations.

The only possible conclusion that a skilled artisan would draw based on these explicit teachings in the application is that the transgenic procedure resulted in a mixed population of genetically identical CICM cells except for the expression or non-expression of a particular transgene.

Therefore, withdrawal of this rejection is believed to be in order as it is not sustainable.

Claims 91, 96 and 97 also stand rejected as only providing enablement support for the expression of LIF as a differentiation inhibiting gene. This rejection is now moot as none of the claims require expression of a gene that inhibits differentiation. Rather, the pending claims merely are directed to CICMs which express a transgene which may be selected from a group of known gene types (claim 97) and do not require that this expression result in a phenotypic change that alters cell differentiation.

Therefore, withdrawal of this rejection is respectfully requested.

Claims 91-100 and 103-105 stand rejected as being in the recital of "the ability of the CICM cells from one cell line being capable of differentially expressing a transgene".

This rejection is traversed. The claims clearly recite a population of cells, comprising one type that expresses a transgene and another population that does not. There is no ambiguity.

Withdrawal of this rejection is respectfully traversed.

Claims 91-95 and 101-05 stand rejected under 35 USC § 102(e) based on Sims. This rejection is respectfully traversed.

As argued in Applicant's last reply, Sims et al does not teach or suggest a mixed population of transgenic totipotent ES cells as claimed. Sims et al does not enable conditions for maintaining a stable CICM cell line in culture, much less a mixed totipotent transgenic cell population as claimed. Rather, Sims suggests that their cells on feeder cells differentiated under the disclosed conditions and that culture in suspension purportedly avoided differentiation. However, in fact, the reverse is true.

Likewise, Sims et al in view of DeBoer et al and Stewart et al does not render obvious the claimed invention. Sims does not for the reasons of record. DeBoer and Stewart et al are cited as respectfully evidence that (i) methods of producing transgenic bovines were known at the time of invention and (ii) methods for producing murine stem cells were also known. This 103 rejection is respectfully traversed.

The fact that methods for producing transgenic bovine cells were known fails to address the fact that methods for producing stable transgenic bovine ES cell lines were not.

Also, the fact that murine ES cell lines were known also does not suggest the claims, as it could not have been extrapolated that conditions appropriate for maintaining murine ES cell line would be applicable to bovine ES cell lines. The reasonable expectation would have been that these different species cells would require different feeder cells, growth factors and other constituents to preclude differentiation. Evidence of the disparities between species is evidenced by the fact that while murine ES do not require feeder layer cultures, human and other primate ES cells must be maintained on a feeder layer to preclude differentiation.

Therefore, based on the foregoing, withdrawal of the § 102 rejection based on Sims and the related § 103 rejection based on Sims in view of Stewart et al and DeBoer et al is respectfully requested.

Based on the foregoing, this application is believed to be in condition for allowance. A Notice to that effect is respectfully solicited.

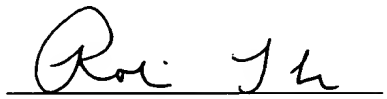
If any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so that prosecution of this application may be expedited.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please

charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #100375.54357DV).

Respectfully submitted,

11/14/2003



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